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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/582,808	10/16/2000	Ib Mendel-Hartvig		2872

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EXAMINER	
COUNTS, GARY W	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 02/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/582,808	MENDEL-HARTVIG ET AL.	
	Examiner	Art Unit	
	Gary W. Counts	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 November 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *42-83* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *42-83* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the claims

The amendment filed November 23, 2004 is acknowledged and has been entered.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

3. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 42, 43, 47, 51-53, 56-57, 59-61, 63, 64, 68, 72-74, 77-78 and 80-82 are rejected under 35 U.S.C. 103(a) as being unpatentable over Charlton et al (US 5,989,921) in view of Batz et al (US 4,415,700) and Brown et al (US 5,149,622).

Charlton et al disclose an immunoassay method for determining the presence of a ligand (analyte) in a sample. Charlton et al disclose applying a sample to an inlet of a test device which comprises a sorbent material which defines a lateral flow path, capable of transporting an aqueous solution by capillary action to a test site (detection zone). Charlton et al disclose that a conjugate comprising a protein bound to a colored particle (Reactant*) is mixed with the sample and inserted into the test device. Charlton et al also disclose that the conjugate may be predeposited in the test strip upstream of the test site (detection zone). Charlton et al disclose that the conjugate and sample flows to the test site (detection zone), which comprises latex particles entrapped or fixed in the flow path having an immobilized protein (antibody)(capturer) on their surface. Charlton et al disclose that if the analyte is present it reacts with immobilized binding protein (antibody) at the test site and forms a sandwich comprising immobilized binding protein-ligand binding protein colored particle (Reactant*) (col 3, line 21 – col 4, line 67). Charlton et al disclose that the color particles have a size of 18 nm (0.018 um) (col 8, lines 16-18). Charlton et al disclose that the beads trapped in the test site have a size of 0.3 microns. Charlton et al also disclose packing the components into a test kit (col 4, line 17). Charlton et al disclose that the test cell can be used to detect any ligand

(analyte) which has been assayed using known immunoassay procedures, or known to be detectable by such procedures (col. 4, lines 29-37).

Charlton et al differ from the instant invention in failing to teach the immobilized particles which exhibit hydrophilic groups on their surface. Charlton et al also fails to specifically teach the particles anchoring the capturer have a size, which is smaller than a smallest inner dimension of the flow channels of the matrix.

Batz et al disclose hydrophilic particles as carrier for biologically and /or immunologically active substances covalently bound to the particle (abstract). Batz et al disclose that the particles can carry substances such as, peptides, proteins, enzymes, hormones, vitamins, antigens, antibodies and micro-organisms (col 5). Batz et al disclose that the use of these hydrophilic particles provides for a diagnostic agent which has covalently bound biological and /or immunological active substances which do not impair the structure and thus the activity of the biologically active proteins (col 2, lines 59-68). Batz also disclose that these hydrophilic particles are especially useful for use in immunoassays (col 5, lines 16-19).

Brown et al disclose a flow device in which particles having a substance capable of reaction with the analyte in the sample, are immobilized in a matrix. Brown et al disclose that the average diameter of the particles is less than the average pore size of the matrix (see abstract). Brown et al disclose that by having the particle sizes having a size which is smaller than the flow channels of the matrix allows for an improved solid-phase analytical device and a binding assay, which provides for a device which is relatively easy to use and require fewer procedural steps and less complex assay

technique (col 4) and is highly advantageous over devices and assay methods of the prior art.

It would have been obvious to one of ordinary skill in the art to substitute the hydrophilic particles as taught by Batz et al for the immobilized latex particles of Charlton et al because Batz et al teaches that these hydrophilic particles can be used as a solid phase in immunoassays and provides for a diagnostic agent which has covalently bound biological and /or immunological active substances which do not impair the structure and thus the activity of the biologically active proteins.

It also would have been obvious to one of ordinary skill in the art to incorporate particles which have a smaller diameter than that of the matrix as taught by Brown et al into the method of Charlton et al because Brown et al shows that by having the particle sizes having a size which is smaller than the flow channels of the matrix allows for an improved solid-phase analytical device and a binding assay which provides for a device which is relatively easy to use and require fewer procedural steps and less complex assay technique and is highly advantageous over devices and assay methods of the prior art.

5. Claims 44-46 and 65-67 are rejected under 35 U.S.C. 103(a) as being unpatentable over Charlton et al., Batz et al., and Brown et al in view of Bennich et al (US 3,720,760).

See above for teachings of Charlton et al., Batz et al., and Brown et al.

Charlton et al., Batz et al., and Brown et al. differ from the instant invention in failing to specifically teach a mixture of biospecific affinity reactants is immobilized to the hydropillic groups on the Capturer Particles.

Bennich et al disclose test allergens immobilized to particles. Bennich et al disclose that these allergens can be allergen extracts. Bennich et al that the test allergen can be a mixture of two or more allergens which provides the advantage whereby a quick "yes" or "no" can be obtained during the examination to the question of whether hypersensitivity against one or more allergens in a large group of allergens is manifest.

It would have been obvious to one of ordinary skill in the art to incorporate test allergens as taught by Bennich et al into the modified method of Charlton et al because Bennich et al shows that the test allergen can be a mixture of two or more allergens which provides the advantage whereby a quick "yes" or "no" can be obtained during the examination to the question of whether hypersensitivity against one or more allergens in a large group of allergens is manifest. Furthermore, Charlton et al disclose that the test cell can be used to detect any ligand which has been assayed using known immunoassay procedure, or known to be detectable by such procedures.

6. Claims 48, 50, 54, 55, 69, 71, 75 and 76 are rejected under 35 U.S.C. 103(a) as being unpatentable over Charlton et al., Batz et al and Brown et al in view of Devlin et al (US 5,846,703).

See above for teachings of Charlton et al., Batz et al., and Brown et al.

Charlton et al., Batz et al, and Brown et al differ from the instant invention in failing to teach the analyte is an antibody of IgE type with specificity to allergens.

Devlin et al disclose that sandwich techniques can also be used to assay antibodies rather than antigens. Devlin et al also disclose determination of an antigen specific IgE by immobilizing antigens to solid phases. The antigens are biospecific for the corresponding antibody. Devlin et al disclose that these IgE antibodies are directed to an allergen (col 2, line 57 – col 3, line 1). Devlin et al disclose that this immunoassay allows for the measurement of antigenic substances in biological materials such as serum, plasma and whole blood and also allows for the determination of an allergen.

It would have been obvious to one of ordinary skill in the art to incorporate the use of immobilized antigens as taught by Devlin et al into the modified method of Charlton et al because Charlton et al disclose that that the test cell can be used to detect any ligand which has been assayed using known immunoassay procedures, or known to be detectable by such procedures and Devlin et al shows that this immunoassay allows for the detection of IgE and also allows for the measurement of antigenic substances in biological materials such as serum, plasma and whole blood and also allows for the determination of an allergen.

With respect to the flow channels having a smallest inner dimension and inner diameter and the particles anchoring the Capturer have a size in the range of 0.4-1000 um as recited in the instant claims, the optimum dimension and diameter of the flow channels and particle size can be determined by routine experimentation and thus would have been obvious to one of ordinary skill in the art. Further, it has long been settled to be no more than routine experimentation for one of ordinary skill in the art to discover an optimum value of a result

effective variable. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum of workable ranges by routine experimentation." Application of Aller, 220 F.2d 454,456, 105 USPQ 233, 235-236 (C.C.P.A. 1955). "No invention is involved in discovering optimum ranges of a process by routine experimentation ." Id. At 458,105 USPQ at 236-237. The "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." Application of Boesch, 617 F.2d 272,276, 205 USPQ 215, 218-219 (C.C.P.A. 1980)

7. Claims 49, 58, 70 and 79 are rejected under 35 U.S.C. 103(a) as being unpatentable over Charlton t al., Batz et al., and Brown et al ., in view of Dafforn et al (US 4,981,786).

See above for teachings of Charlton et al., Batz et al., and Brown et al.

Dafforn et al disclose the application of reagents upstream of a sample application site (col 13, lines 32-44) and also disclose detecting autoimmune antibodies (col 5, lines 1-8). Dafforn et al disclose that the application of reagents in this manner and the detection of autoimmune antibodies provides for a device which is simple, rapid, accurate, and safe and avoids contamination of various reagents during their addition to the device (col 2, lines 32-42) and provides for the detection of clinically important proteins (col 4, lines61-68).

It would have been obvious to one of ordinary skill in the art to incorporate the application of reagents and the detection of autoimmune antibodies as taught by Dafforn et al into the modified method of Charlton et al because Dafforn et al shows that the application of reagents in this manner and the detection of autoimmune antibodies

provides for a device which is simple, rapid, accurate, and safe and avoids contamination of various reagents during their addition to the device and provides for the detection of clinically important proteins.

8. Claims 62 and 83 are rejected under 35 U.S.C. 103(a) as being unpatentable over Charlton et al, Batz et al and Brown et al in view of Self et al (US 4,446,231).

See above for teachings of Charlton et al, Batz et al and Brown et al. Charlton et al, Batz et al and Brown et al differ from the instant invention in failing to teach the diagnosis of an autoimmune disease.

Self et al disclose that immunoassays are used for the detection and/or determination of autoimmune diseases. Self et a disclose shows that immunoassays have a wide application, in both clinical and non-clinical fields and that they are particularly useful in any circumstance where it is necessary to detect and/or determine small or very small amounts of substances.

It would have been obvious to one of ordinary skill in the art to use immunoassays as taught by Self et al for the diagnosis of autoimmune diseases because Self et al show that immunoassays are used for the detection and/or determination of autoimmune diseases and that immunoassays have a wide application, in both clinical and non-clinical fields and that they are particularly useful in any circumstance where it is necessary to detect and/or determine small or very small amounts of substances. Furthermore, Charlton et al disclose that the test cell can be used to detect any ligand which has been assayed using known immunoassay procedures, or known to be detectable by such procedures.

Response to Arguments

9. Applicant's arguments filed November 23, 2004 have been fully considered but they are not persuasive.

Applicant argues that Charlton et al does not teach or suggest a method or test kit as defined in claims 42 and 63 wherein a biospecific affinity reactant (Capturer) is firmly anchored to a flow matrix via immobilized particles exhibiting hydrophilic groups on their surface, particularly in combination with an analytically detectable reactant (Reactant*) having labeled particles as an analytically detectable group. Applicant argues that the hydrophobic particles of Charlton et al absorbed very strongly to flow matrices such as nitrocellulose membranes and that the hydrophobic features of the particles promote non-specific absorption of an analytically detectable reactant (Reactant*) and/or analyte and therefore decrease the sensitivity of test methodologies. Applicant argues that Charlton does not teach or suggest immobilized particles exhibiting hydrophilic groups on their surface. This is not found persuasive because the Examiner has not relied upon Charlton et al for teaching this limitation but rather has relied upon Batz et al for teaching the advantages of hydrophilic particles in binding assays and for their advantages over hydrophobic particles used in binding assays. Furthermore, Charlton et al disclose that any ligand which has heretofore been assayed using known immunoassay procedures or known to be detectable by such procedures can be used (col 4).

Applicant argues that the deficiencies of Charlton et al are not resolved by Batz et al. Applicant argues that Batz et al does not teach or suggest a flow matrix

immunoassay or use of the latex particles described therein in a flow matrix immunoassay. This is not found persuasive because Examiner has not relied upon the Batz et al reference for this limitation but rather has relied upon Charlton et al for teaching this limitation. Applicants state that there is no teaching or suggestion by Batz et al that their latex particles are suitable for adsorbtion to a second solid support or matrix. This is not found persuasive because although Batz et al does not specifically suggest that their latex particles are suitable for adsorption to a second solid support or matrix it is within the realm of one of ordinary skill in the art to replace one solid phase particle having immobilized biospecific affinity reactant for another solid phase particle comprising a biospecific affinity reactant because the use of solid phase particles in binding assays is very well known in the art.

In response to applicants argument that Batz et al does not teach or suggest their particle will provide improved sensitivity in flow matrices and decrease the tendency of non-specific absorption in a detection zone as is obtained according to the present invention. In response to applicant's argument that Batz et al does not teach or suggest their particle will provide improved sensitivity in flow matrices and decrease the tendency of non-specific absorption in a detection zone as is obtained according to the present invention, the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985).

Applicant argues that Brown et al fail to teach that the particle size is smaller than the flow channels of the matrix or, as required by the present claims, that the particles have a diameter smaller than a smallest inner dimension of the flow channels of the flow matrix. This is not found persuasive because Brown et al specifically teaches that the average diameter of the particles is less than the average pore size of the matrix (abstract) and as stated in the previous office action the optimum dimension and diameter of the flow channels and particles size can be determined by routine experimentation and thus would have been obvious to one of ordinary skill in the art. Therefore, it is the Examiner position that the combination of Brown et al with Charlton et al and Batz et al is appropriate and thus reads on the instantly recited claims.

Applicant argues that Devlin et al does not teach or suggest a method or test kit as presently claimed or for modifying the teachings of Charlton et al to provide such a method or test kit. Particularly, applicants find not teaching or suggestion by Devlin et al for a method or test kit employing a flow matrix as presently claimed wherein an analytically detectable reactant (Reactant*) has labeled particles as an analytically detectable group and a biospecific affinity reactant (Capturer) is anchored to the flow matrix via immobilized particles of a size and function as claimed and exhibiting hydrophilic groups on their surface. This is not found persuasive because Examiner has not relied upon Devlin et al for these limitations but rather has relied upon Charlton, Batz and Brown for these limitations. Examiner has relied upon Devlin for teaching immunoassay procedures for determining an analyte of interest. Furthermore, Charlton

et al disclose that the test cell can be used to detect any ligand which has been assayed using known immunoassay procedures, or know to be detectable by such procedures.

Applicant argues that Dafforn, does not teach or suggest a method or test kit employing a flow matrix as presently claimed wherein an analytically detectable group reactant has labeled particles as an analytically detectable group and a biospecific affinity reactant is anchored to the flow matrix via immobilized particles exhibiting hydrophilic groups on their surface. This is not found persuasive because Examiner has not relied upon the tertiary reference for these limitations. The above limitations are taught by the combination of the primary and secondary references. Examiner has relied upon Dafforn for the application of reagents upstream of a sample applicant and the advantages of this type of application (see previous office action).

Applicant argues that Self broadly discloses an immunoassay using an amplified cyclic detection system and that Self does not teach or suggest the limitations as recited in claims 42 and 63 and that the combination of Charlton et al, Batz et al, Brown et al and Self does not enable one of ordinary skill in the art to conduct the presently claimed method or to make and sue the presently claimed methods and test kits obvious. This is not found persuasive because as stated in the previous office action and above Self et al show that immunoassays are used for the detection and/or determination of autoimmune diseases and that and that immunoassays have a wide application, in both clinical and non-clinical fields and that they are particularly useful in any circumstance where it is necessary to detect and/or determine small or very small amounts of substances. Furthermore, Charlton et al disclose that the test cell

can be used to detect any ligand which has been assayed using known immunoassay procedures, or known to be detectable by such procedures.

Conclusion

10. No claims are allowed.

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary W. Counts whose telephone number is (571) 272-0817. The examiner can normally be reached on M-F 8:00 - 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gary W. Counts
Examiner
Art Unit 1641
February 11, 2004

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02/20/04